An Approach to Mediastinal Masses Associated with Hyperthyroidism*

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Benign thymic hyperplasia (BTH) is a known feature of hyperthyroidism, but is infrequently appreciated by clinicians. In most cases thymic enlargement is minimal; however, it may occasionally present as an appreciable anterior mediastinal mass. While surgical resection is a common approach to such a mass, recognition of the benign nature of BTH and its regression following treatment of hyperthyroidism would prevent a major surgical procedure. We present three cases of BTH associated with hyperthyroidism and describe our approach to this syndrome.

Benign thymic hyperplasia (BTH) is a known feature of Graves’ disease, but this association is better known to the pathologist than the clinician. In most cases, thymic enlargement is minimal and inapparent. However, newer imaging techniques such as computed tomography, or the rare patient with massive thymic enlargement may present to the clinician the dilemma of thyroid disease coincident with an anterior mediastinal mass. While median sternotomy and surgical resection is a common approach to mediastinal masses, BTH has been shown to regress following treatment of hyperthyroidism, although only a single case report describes this approach to a patient with radiologic evidence of an anterior mediastinal mass. Recognition of the association of massive thymic hyperplasia with hyperthyroidism (HTH) and the benign course following treatment for HTH would prevent a major surgical procedure.

We present three patients with BTH associated with HTH; in two, treatment of the hyperthyroid state resulted in prompt regression of the thymus. These patients illustrate an evolution in approach to this syndrome.

**CASE REPORTS**

Patient 1 is a 29-year-old woman admitted to the University of Chicago Hospitals and Clinics with a six-month history of weight loss, hyperphagia, palpitations, hair loss, insomnia, night sweats, irregular menstrual periods and increasing weakness. The patient had a history of anemia due to beta thalassemia minor and no family history of thyroid disease. Her physical examination was notable for tachycardia, bilateral lid lag and exophthalmos, and a diffusely enlarged, non-nodular thyroid. There was no lymphadenopathy or splenomegaly. Thyroid function testing demonstrated the thyroid level (T4) to be 22.1 µg/dl, the free thyroxine index (FTI), defined as the total T4 times the resin-uptake ratio 32.3 (normal range 6.0-10.5), and the triiodothyronine level 532 ng/dl. Chest roentgenogram revealed an anterior mediastinal mass. Thyroid scan demonstrated diffuse uptake without a retrosternal thyroid, and the radioiodine uptake was 50 percent. Antithyroglobulin and antimicrosomal antibodies were absent. The patient was treated with propylthiouracil (PTU) 200 mg qid and Lugol’s solution 10 drops tid for three weeks.

Computed tomography (CT) scan of the chest revealed an unenhancing, solid anterior mediastinal mass contiguous with the pericardium and obliterating the periaortic and paracaval fat planes. The mass did not extend cephalad to the goiter. Result of a gallium scan was normal. Due to concerns about a malignant thymoma, the patient underwent a thymectomy via a median sternotomy concurrent with a subtotal thyroidectomy. The thymus weighed 150 grams; microscopic examination revealed thymic hyperplasia with very occasional lymphoid follicles and plasma cells. Antithyroid medication was discontinued after surgery. The patient had an uneventful recovery and course.

Patient 2 is a 50-year-old woman with a nodular goiter diagnosed at age 32 who underwent subtotal thyroidectomy 11 years prior to presentation. Two years before admission, she developed angina; chest roentgenographic findings at the time were normal. The patient continued to have symptomatic coronary artery disease and eventually presented to the University of Chicago Hospital and Clinics with prolonged chest pain and a history of fatigue, weakness, thinning hair, and tremor. During admission and evaluation the patient was found to have an enlarged, nodular right thyroid. The T4 uptake was 15.7 µg/dl and the FTI 23.2. No retrosternal uptake was seen on thyroid scan. Uptake by the right thyroid was 55 percent. Chest roentgenogram showed an anterior mediastinal mass, confirmed by CT scan (Fig 1). Result of a gallium scan was normal. Tests for antithyroglobulin and antimicrosomal antibodies were negative.

The patient underwent parasternal mediastinoscopy and biopsy of the thymus gland, which demonstrated normal thymic tissue and spared the patient a major operation. She was then treated with PTU 100 mg qid and propranolol 40 mg qid. After six months, a repeat CT scan showed minimal anterior mediastinal widening (Fig 2) with regression of thymic enlargement. Two years after initial evaluation the patient continues on antithyroid therapy at the same dosage without incident.

Patient 3 is a 17-year-old girl admitted with a six-month history of weight loss, nervousness, fatigue, insomnia, neck swelling, hair loss, palpitations, and polyphagia. On examination there was an enlarged, non-nodular thyroid but no lid lag or exophthalmos. The T4 uptake was 23.6 µg/dl and the FTI was 29.1; antimicrosomal antibodies were

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present in a titer of 1:20,480, but antibodies to thyroglobulin were absent. Chest roentgenogram revealed an anterior mediastinal mass. Chest CT confirmed the mass extending from the thoracic inlet to the aortic arch. No retrosternal thyroid was seen.

The patient was treated with propranolol 10 mg qid and PTU 100 mg tid with amelioration of her hyperthyroid state. A repeat chest CT six months later showed a diminished anterior mediastinal mass. Two years after initial evaluation the patient continues on propranolol 30 mg tid and PTU 50 mg tid without complications.

DISCUSSION

The differential diagnosis of an anterior mediastinal mass includes a number of entities and in a young adult, may prompt surgery for diagnosis and/or treatment. With the exception of lymphomatous involvement of the mediastinum, many would consider median sternotomy and resection appropriate for both diagnosis and therapy. Benign thymic hyperplasia has been found in association with hyperthyroidism in a few cases over the past 60 years.1,2,4,6 It is by no means common, however, and is not emphasized in major endocrinology texts. Yet pathologically, approximately one third of patients with thyrotoxicosis will have microscopic abnormalities of the thymus gland with the presence of medullary lymph follicles upon biopsy.4 Recognition of the association of BTH and HTH and regression of the thymus following treatment of the hyperthyroid state may preclude the need for an invasive diagnostic or therapeutic procedure.

Our series serves to illustrate the evolution of our approach to such patients. The first patient underwent thymectomy to exclude thymoma or other malignancy. In patient 2, recognition of the association of thymic hyperplasia with HTH, as further confirmed by biopsy, spared the patient further surgery. In both patients 2 and 3, successful treatment of HTH resulted in involution of the enlarged thymus gland.

The mechanism of thymic enlargement in hyperthyroidism is not well established. B-cell lymphocytes produce an IgG immunoglobulin responsible for the hyperplasia and hyperactivity of the thyroid gland in Graves' disease. There is some evidence that T-cell lymphocytes also have a supportive role in this disorder.4 However, removal of the thymus gland in a patient with both thyimic hyperplasia and Graves' disease did not ameliorate the patient's HTH.4 The thymus of that patient neither contained nor synthesized the LATS immunoglobulin. Alternatively, thymic hyperplasia may be caused by excess thyroid activity. Thyroidectomy has been associated with thymic involution, and administration of triiodothyronine can induce thymic hyperplasia.4 Treatment with antithyroid drugs, including propranolol, may cause a decrease in thymic enlargement in man, either by direct effect on the thymus or by control of hyper-

Figure 1. CT scans confirm anterior mediastinal mass.

Figure 2. Six months following treatment of hyperthyroidism, there is resolution of the mediastinal abnormality.
In summary, BTH may be a direct consequence of hyperthyroidism and return to a euthyroid state is associated with resolution of thymic enlargement. Therefore, we believe that median sternotomy and resection is inappropriate in patients with an anterior mediastinal mass and hyperthyroidism. Treatment with appropriate antithyroid therapy should result in regression of the thymus. Invasive diagnostic procedures such as mediastinoscopy can be used when regression does not occur or when there is a clinical suspicion of another process in the mediastinum.

References
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